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A Prospective Study of Disease Patterns and Assessment of Drug Interactions with Prasugrel in Tertiary Care Hospital Patients

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Abstract

This prospective observational study evaluates the prescribing patterns and drug-drug interactions of Prasugrel in hospitalized patients at a tertiary care hospital (BBH). Conducted over six months, it involved 110 inpatients, gathering data from various sources including patient profiles, medicine charts, and lab tests. The study primarily focused on Prasugrel usage, identifying patient demographics and assessing the interactions of Prasugrel with other medications. It found that 64.02% of the patients on Prasugrel therapy were male and 36.08% female, predominantly aged between 55 to 75 years. These patients often had a history of cardiovascular and infectious diseases. The study revealed that 31.36% of patients experienced interactions with Prasugrel, with a higher incidence in males. The most common interactions were with Pantoprazole, Omeprazole, and Aspirin. These interactions were classified as severe (11.81%), moderate (55.05%), and mild (34.13%). Additionally, 17.91% of interactions were defined, 58.45% probable, and 22.62% possible. Prasugrel was mainly prescribed for heart disease, myocardial infarction, and angina. The study suggests cautious use of Pantoprazole with Prasugrel due to potential significant interactions.

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INTRODUCTION

In earlier reports, the drug-drug interaction profile of prasugrel was primarily concerned with the combination therapy of prasugrel with a number of other western medications, such as digoxin, fluoxetine, morphine, caffeine, ritonavir, cyclosporine, rifampicin, sibutramine, and efavirenz. Abrocitinib: substances having antiplatelet qualities may intensify abrocitinib's antiplatelet effects [1]. For the first three months of abrocitinib therapy, avoid using antiplatelet medications in combination with abrocitinib. This

combination is forbidden according to the medical advice for abrocitinib. Low dosage aspirin (81 mg/day or less) is exempt from this. It should be avoided in combination since it is categorised as risk X. Agents with antiplatelet characteristics may have their antiplatelet effects amplified by acalabrutinib. It requires therapeutic monitoring and is categorised as risk C. Antiplatelet medications, such as P2Y12 inhibitors, NSAIDs, SSRIs, and others, have the potential to amplify the antiplatelet effects of other treatments that also possess these characteristics. It requires therapeutic monitoring and is categorised as risk C [2].

Amiodarone

This may decrease serum concentrations of the active metabolite(s) of Prasugrel. It is classified as risk c and needs monitor therapy.

Amodiaquine

The serum concentration of amodiaquine may rise in response to moderate CYP2C8 inhibitors. It is categorised as Risk X and must be avoided in combination. Anticoagulants: Antiplatelet agents may intensify anticoagulants' anticoagulant effects. It is categorised as risk C and requires therapeutic monitoring.

Bupropion

Weak CYP2B6 Inhibitors may raise the level of bupropion in the serum, and the risk classified as C, which needs the monitor of therapy [3].

Alpelisib

Alpelisib's serum levels may rise as a result of BCRP/ABCG2 inhibitors. Management: Steer clear of co-administering alpelisib and BCRP/ABCG2 inhibitors as this may lead to elevated alpelisib concentrations and toxicities. If co-administration is unavoidable, it needs to be closely watched for a rise in adverse reactions to alepelisib. It is classified as risk d and need to consider therapy modification.

Apixaban

Apixaban's harmful or hazardous effects could be exacerbated by antiplatelet agents (P2Y12 Inhibitors). In particular, there can be a higher chance of bleeding. Canadian labelling advises against using ticagrelor or prasugrel; while managing this combination, carefully weigh the benefits and hazards and keep a tight eye on things. It is classified as risk D and considered therapy modification.

Calcium Channel Blockers

This could lessen the benefits of prasugrel as medicine. Therapy needs to be closely monitored because it is identified as risk C. Prasugrel's active metabolite(s) may be more concentrated in the serum when CYP2C19 Inducers (Strong) operate. Wherever possible, management should take into account alternatives to this mix. If Prasugrel is taken alongside a potent CYP2C19 inducer, keep an eye out for any harmful effects (like bleeding) and increased Prasugrel effects. Consider modifying your therapy; this is referred to as risk D [4].

Dabigatran Etexilate

Dabigatran etexilate may have a more harmful or toxic effect when used with antiplatelet agents (P2Y12 Inhibitors). In particular, there can be a higher chance of bleeding. Dabigatran etexilate serum concentrations may rise in response to antiplatelet agents (P2Y12 Inhibitors). More specifically, dabigatran serum concentrations may rise with prasugrel. Canadian labelling advises against using ticagrelor or prasugrel; in management, carefully weigh the advantages and disadvantages of this combination and keep a tight eye on things. It is regarded as therapeutic modification and is designated as risk D.

CYP2C19 Inhibitors (Moderate)

may lower blood levels of the medication prasugrel's active metabolite(s). It is classified as risk C and needs monitor of therapy.

CYP2C19 Inhibitors (Strong)

May lower the levels of the active metabolite(s) of prasugrel in serum. Managers should, whenever feasible, look into alternatives to this combo. Patients should be cautiously watched for signs of a decreased response to pransugrel if such a combination is necessary. Treatment modification is the classification, with risk level set at D [5].

Dasabuvir

The serum concentration of dasabuvir may rise in response to moderate CYP2C8 inhibitors. Risk C is applied, and therapy needs to be monitored.

Edoxaban

Edoxaban's harmful or hazardous effects could be amplified by antiplatelet agents (P2Y12 Inhibitors). That is, there could be a higher chance of bleeding. Carefully weigh the expected advantages and hazards of this combination in management. Combining both calls for closer attention to any bleeding. They do take therapeutic modification into consideration and classify it as risk D.

Enzalutamide

The concentration of Enzalutamide's active metabolite(s) in the serum may rise in response to moderate CYP2C8 inhibitors. Elevated serum concentrations of enzalutamide may be caused by moderate CYP2C8 inhibitors. It requires monitoring and therapy because it is categorised as risk C. Systemic erythromycin: May lessen prasugrel's antiplatelet action. It is classified as risk C and needs to monitor of therapy [6].

Enoxaparin

The anticoagulant activity of enoxaparin may be strengthened by substances having antiplatelet properties. Whenever possible, stop using antiplatelet medications before starting enoxaparin in management. If simultaneous administration cannot be avoided, keep a close eye out for any bleeding symptoms. It is categorised as risk D and takes therapeutic modification into account.

Esomeprazole

This could reduce the antiplatelet effects of prasugrel. The levels of Prasugrel's active metabolite(s) in the blood may drop when taking esomeprazole. It is classified as risk X therefore it needs to avoid combination.

Rivaroxaban

Rivaroxaban's harmful or toxic effects could be exacerbated by antiplatelet agents (P2Y12 Inhibitors). More specifically, there can be a higher chance of bleeding. Canadian labelling advises against using ticagrelor or prasugrel; in the management, carefully weigh the advantages and disadvantages of this combination and keep a close eye on things. It falls under risk category D, and therapeutic adjustment should be considered [7].

Rosuvastatin

It is necessary to monitor therapy as rosuvastatin serum concentrations may rise due to prasugrel, which is categorised as risk C. Salicylates: Salicylates can have a harmful or toxic effect, which can be increased by substances having antiplatelet characteristics. Bleeding risk may increase as a consequence. It requires therapeutic monitoring and is categorised as risk C.

Fentanyl

May lessen antiplatelet agents' antiplatelet effects (P2Y12 Inhibitors). The serum concentration of antiplatelet agents (P2Y12 Inhibitors) may be lowered by fentanyl. It is categorised as risk C, requiring close monitoring during treatment. Grapefruit juice: May lower blood levels of the active metabolite(s) of prasugrel. It is advisable for medical professionals to counsel Prasugrel-using patients to limit their intake of grapefruits and grapefruit juice. Three 200 mL glasses of grapefruit juice per day may significantly lessen the antiplatelet effects of prasugrel. It is categorised as risk D and takes therapeutic modification into consideration [8].

Pantoprazole

may reduce the amount of Prasugrel's active metabolite(s) in the blood. When it comes to management: Clinicians should carefully examine whether proton pump inhibitor medication is necessary for patients receiving Prasugrel, given the potential risk of decreased Prasugrel effectiveness. This interaction does not seem to be present in other acid-lowering treatments. It is categorised as risk C, and treatment is being monitored.

Omeprazole

May diminish the antiplatelet effect of Prasugrel. Omeprazole may decrease serum concentrations of the active metabolite(s) of Prasugrel. It is classified as risk X and needs to be avoiding from combination.

Morphine (Systemic)

This might reduce the antiplatelet action of P2Y12 inhibitors, or antiplatelet agents. The blood level of antiplatelet agents (P2Y12 Inhibitors) may drop when taking systemic morphine. If at all possible, individuals with acute coronary syndromes

treated with P2Y12 inhibitors should also be considered for alternate anti-ischemic/analgesic therapy (such as beta-blockers or nitroglycerin). Unknown are the dangers connected to other opioids. It is classified as risk D and considered therapy modification [9].

Omega-3 Fatty Acids

may strengthen the antiplatelet effects of substances possessing antiplatelet characteristics. categorised as risk C and requires therapeutic supervision. Agents possessing antiplatelet characteristics may have their antiplatelet action amplified by multivitamins and minerals (without iron, with AE). assigned a risk classification of C and therapy is being monitored.

Lansoprazole

may lower blood levels of the medication prasugrel's active metabolite(s). It requires therapeutic monitoring and is categorised as risk C. Heparin: Antiplatelet agents may strengthen Heparin's anticoagulant activity. If coadministration of heparin or an antiplatelet drug is necessary, the dose of these medications should be decreased. It is categorised as risk D and is thought to include a change in therapy. Uncertain explanations for a poor response to prasugrel have been reported; nonetheless, aspects related to genetics, metabolism, cellular function, and clinical state have been suggested. Prodrugs include prasugrel. Because of variations in intestinal absorption and cytochrome P450 isoenzyme availability and/or activity, it is thought that decreased production of its active metabolite leads to low Prasugrel response [10]. One possible interaction with prasugrel is a medication that decreases the availability of the active metabolite of prasugrel, which will limit the latter's capacity to induce platelet inhibition. This holds significance since a diminished reaction to Prasugrel escalates the likelihood of significant adverse cardiac events, including but not limited to stent thrombosis, repeated acute coronary syndrome, cardiovascular mortality, and recurrent revascularization. Proton pump inhibitors (PPIs), which are often used, and prasugrel have been linked to a possible interaction. Patients undergoing antiplatelet therapy frequently take 11 PPIs for gastrointestinal bleeding prophylaxis. In a Clinical Expert Consensus Document published in 2008 by the American Heart Association (AHA), American College of Cardiology, and American College of Gastroenterologists. For patients who have experienced previous gastrointestinal bleeding, PPI medication combining aspirin and prasugrel is recommended [11]. In reality, each year, 100 million prescriptions for Prasugrel and PPIs are written. Nevertheless, since omeprazole is accessible over-the-counter in some strengths, this does not cover all uses of the medication. It has been suggested that using PPIs in addition to Prasugrel may raise the risk of serious adverse cardiac events.

Table 1 Prasugrel Information [12]

Trade Names	Plavix, Iscover, Others
Pregnancy Category	AU : B1
Routes of administration	By mouth
Bioavailability	≥79%
Protein binding	Active metabolite: ~98%
Metabolism	enzymatic
Onset of Action	30 mnts
Elimination half life	~7 h (range 2 h to 15 h)
Excretion	Urine (~68% inactive metabolites); feces (27% inactive metabolites)
Formula	$C_{20}H_{20}FNO_3S$
Pharmacologic Category	Anti-platelet medication

Primary Objective

A. To assess the prescribing pattern of the Prasugrel among in-patients a tertiary care hospital.

B. To assess drug- drug interactions with Prasugrel at a tertiary care hospital.

Secondary Objective:

A. To evaluate the severity of interactions among patients used Prasugrel.

B. To evaluate the possibility of relations between Prasugrel and its interactions in patients hospitalized [13].

METHODOLOGY:

Study Design:

This is a prospective observational study carried out at a tertiary care hospital's inpatient departments.

Source of data and Materials:

- Inpatient prescription
- Medication chart
- Medication history chart
- Medicine strips
- Medication history interview

Inclusion Criteria:

- Pediatric patient are not taken into consideration.
- Pregnancy women
- Patients in OP department.
- Patients considered as poisoned diagnosis.

Exclusion Criteria:

- All non-pregnancy patients hospitalized in hospital
- Patients with age of greater than 18 years old
- Both genders male and female.

Sample Size:

This clinical study is done on 110 hospitalized patients at BBH, which patients and their information is collected according to the needs of the study [14].

Method of collection of data

A data collection form prepared base on objectives and data required to be collected. This data collected from patients profile, medicine chart, nurse notes, daily doctor's reports of patients, lab tests and other additional information. All of this detail collected from patients who are used Prasugrel in their treatment. Data collection form is made of two parts, one of it is related to the patients' information and prescription of Prasugrel and other part is related to interactions of Prasugrel and scales to evaluate the interactions. Data collection is done till the patient is discharged from the hospital by any reason. During collection of data for any patient was monitor for total days in hospital to evaluate interactions of Prasugrel. When the data collected completely per patient it entered to computer software named excel which prepared based of data collection form and requests for study. In this study we used similar articles, textbooks, websites, and valid software such as Micromedex and Medscape as tools to reach better result of study [15].

Study procedure:

On a predetermined data collecting form, all medically relevant information is recorded. Conversely, the patient's demographic information and comprehensive medical history, including previous, present, family, personal, as well as drug history recorded in data collection form. The other details like the present diagnosis, reason for the present admission also noted with in duration of 6 month. Patients of both genders who are admitted into the inpatient wards in the Hospital, in age greater than 18 years are include in the study [16]. A professional form prepared with all of details about interactions to study about the Prasugrel interactions; for prove of the drug interactions DIPS scale have been used to see the probability. And also a differential scale used to evaluate the severity of interactions based on the Medscape and Micromedex scales. After completion of data collection on patients, they enter to excel software and used to prepare results based on the objectives [17].

Statistical analysis

The study utilised descriptive statistics to calculate the mean, standard deviation, frequency, and percentage of patient demographic and clinical features, as well as medication-related data. For data analysis, Windows version 22.0 of the Statistical Package for Social Sciences was utilized [18].

Study period

The study and data collection carried out for a period of 6 month (24 weeks)

Study site

The study is done in the inpatient departments of ----------

RESULTS AND DISCUSSION:

This study is conducted on 110 patients at ----------, a tertiary care hospital. 64.02% of these patients were male and 36.08% of these patients were female (table 2) (figure 1).

Table 2 Patients Based on the Gender

Gender	Number	Percentage
Total	110	100%
Male	70	64.02%
Female	40	36.08%

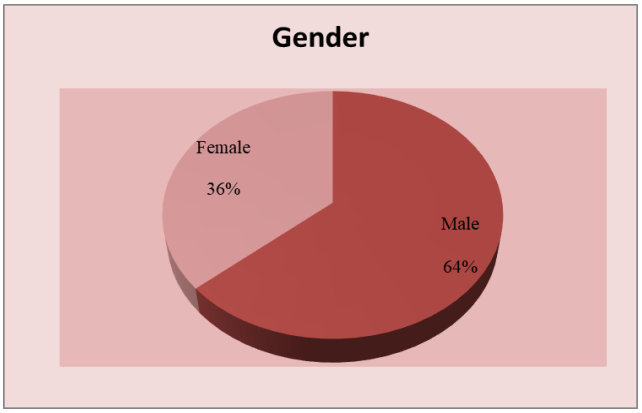

Figure 1: Evaluation of patients based on the gender

In other hands, patients are classified into 8 groups of ages to evaluate the population of patients considered to use of Prasugrel; according to data collected on these patients, most of patients were under Prasugrel therapy were in ages between 55 to 75 years old (table 3) (figure 2).

Table 3 Classification of patients based on the age

Age	Number	Percentage
18-25	2	3.31%
26-35	10	9.38%
36-45	16	11.66%
46-55	18	17.69%
56-65	23	24.42%
66-75	26	20.01%
76-85	12	10.1%
86-95	3	2.58%

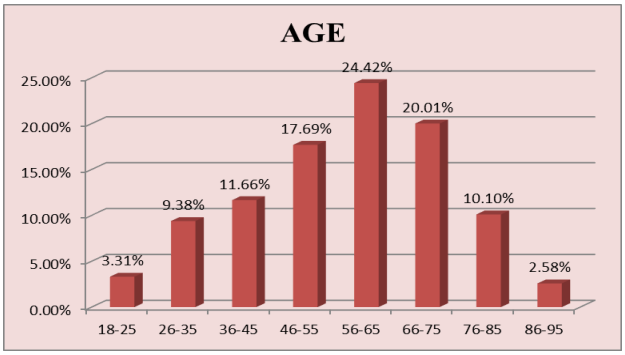

Figure 2: Evaluation of Patients Based on the Ages

Also patients are evaluated according to their past history of diseases. Therefore based on the data, 11.98% of patients had nervous system diseases, 74.38% of patients had cardiovascular diseases, 25.69% of patients had respiratory tract system diseases, 3.80% cancer, 20.04% history of surgery, 18.63% had hormonal and glands diseases, 37.25% had muscle and skin diseases, 8.52% fractures and bones conditions, 19.50% gastrointestinal system disease, 25.41% urinary tract diseases, 47.60% infection diseases and 12.1% of patients had rare and different situations which were not included in above categories (table 4) (figure 3).

Table 4 Population History of disease

Past History	Number	Percentage
Nervous system Diseases	12	11.98%
Cardiovascular Disease	92	74.38%
Respiratory Tract System Diseases	32	25.69%
Cancer	3	3.80%
Surgery	23	20.04%
Hormonal and Glands Disease	22	18.63%
Muscle and Skin Diseases	45	37.25%
Fractures and Bones Condition	11	8.52%
Gastrointestinal System Disease	21	19.50%
Urinary Tract Diseases	28	25.41%
Infectious Diseases	57	47.60%
Other Rare Situations	12	12.1%

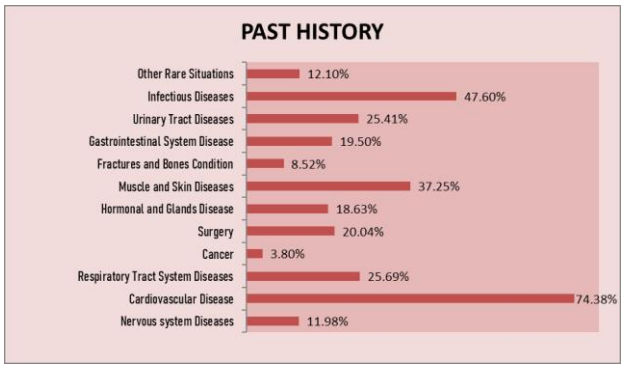

Figure 3: Evaluation of Population History of Diseases

Out of 110 patients used Prasugrel, 28.63% interactions identified with Prasugrel and other drug on their treatment and 71.36% of patients

had no history of interaction with Prasugrel during their interactions (table 5) (figure 4).

Table 5 Population of Interactions

Interactions	Number	Percentage
Total Population	110	100%
Total Patients with Interactions	28	28.63%
Total Patients without Interactions	82	71.36%

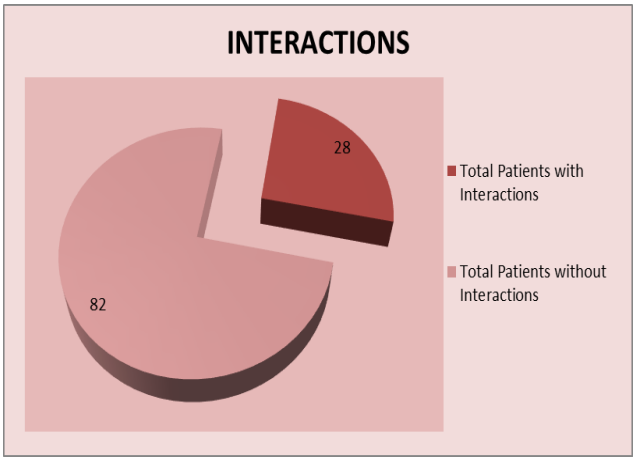

Figure 4: Population of Interactions

Among 37 patients found with Prasugrel interactions, 74.32% of them classified with in male categorize and 25.67% of them into female categorize. Therefore males were the most exposed to Prasugrel; interaction on their treatment (table 6) (figure 5).

Table 6 Interactions Based on the Gender

Interactions	Number	Percentage
Male	28	74.32%
Female	9	25.67%

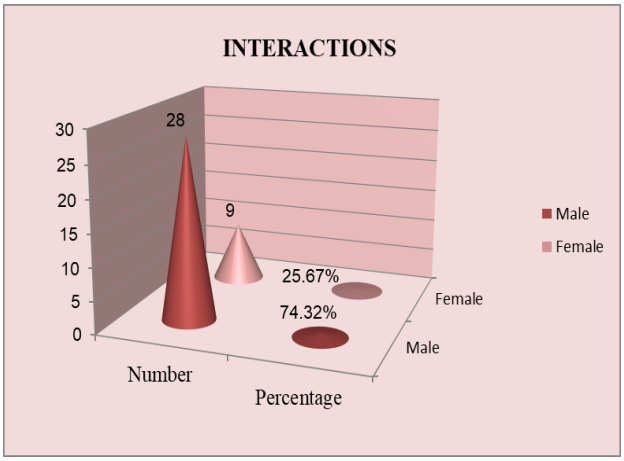

Figure 5: Population of the Interactions Based on the Gender

Based on the data collected in these study, Prasugrel had interactions with Omeprazole (15.21%), Aspirin (17.21%), Hydrocortisone (9.1%), Pantoprazole (16.91%), Metronidazole (10.1%), Budesonide 12.51%), Heparin (3.7%), Repaglinide (1.7%), Fluconazole (3.7%), Phenytoin and Cyclosporine (2.7%) (table 7) (figure 6).

Table 7 Drug Interactions with Prasugrel

Interaction With	Number	Percentage
Omeprazole	7	15.21%
Aspirin	5	17.21%
Hydrocortisone	2	9.1%
Pentaprazole	8	16.91%
Metronidazole	2	10.1%
Budesonide	5	12.51%
Heparin	2	3.4%
Repaglinide	1	1.7%
Fluconazole	2	3.7%
Phenytoin	1	2.7%
Cyclosporine	2	3.7%

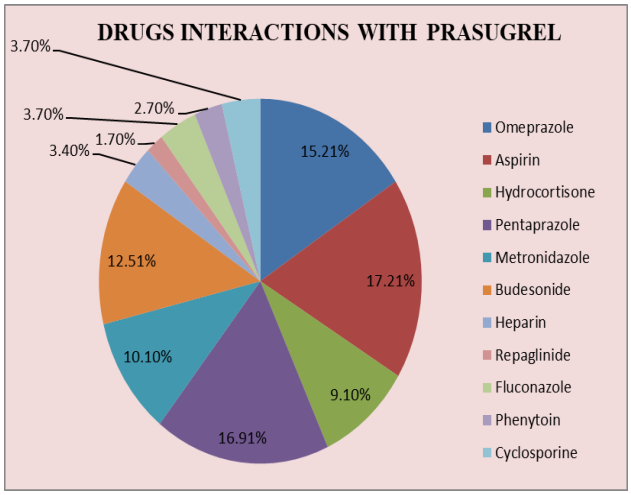

Figure 6: Evaluation of drug interactions with Prasugrel

Based on the evaluation in this study on interaction with use of scales, 11.05% were identify as severe interactions, 53.81% were classify and identify as moderate in their interactions and 34.13% were classify as mild in their interactions (table 8) (figure 7).

Table 8 Severity of Interactions

Titles	Number	Percentage
Severe	6	11.05%
Moderate	18	53.81%
Mild	13	34.13%

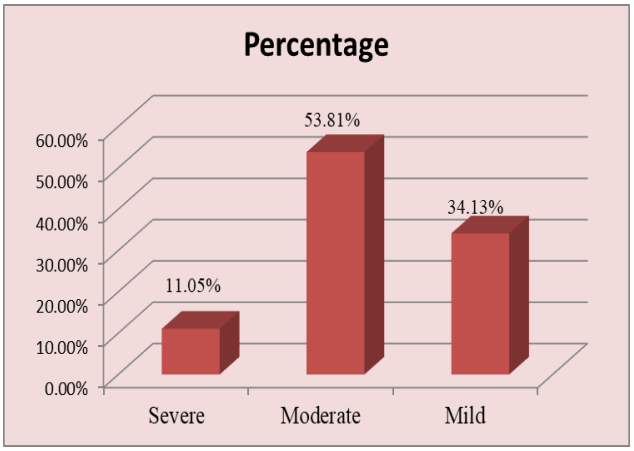

Figure 7: Evaluation and severity of Interactions

In other hand we evaluate interaction based on their possibility of relation the effect and interactions, whereas we found that 17.62% of interaction were defined, 60.46% of interactions were probable and 22.91% of them were possible (table 9) (figure 8).

Table 9 Probability of Interactions

Titles	Number	Percentage
Defined	8	17.62%
Probable	20	60.46%
Possible	9	22.91%

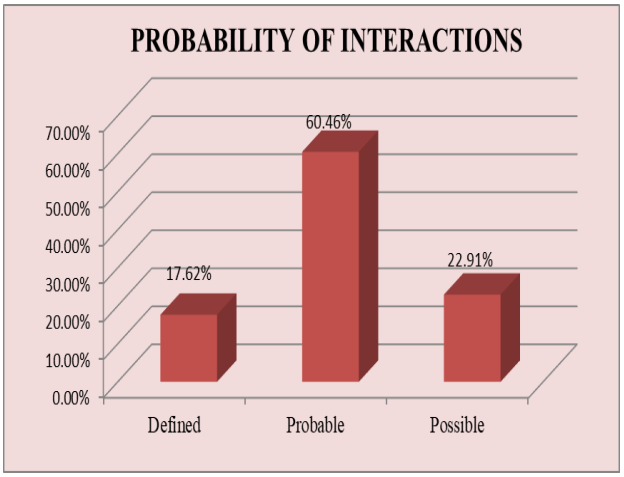

Figure 8: Evaluation and Probability of Interactions

Prasugrel used for several indication or target of actions, these indications could be named as Heart Disease (42.58%), Myocardia Infraction (33.66%), Angina (17.92%), Coronary Artery Bypass Surgery (2.26%), Stroke (8.34%), Artery Atherosclerosis (4.96%) and other unknown condition (5.31%) (Table 10) (Figure 9).

Table 10 Classification of Indications Use for Prasugrel

Diseases Name	No of Patient	Percentage
Heart Disease	52	42.58%
Myocardia Infraction	44	33.66%
Angina	21	17.92%
Coronary Artery Bypass Surgery	2	2.26%
Stroke	13	8.34%
Artery Atherosclerosis	5	4.96%
Unknown	8	5.31%

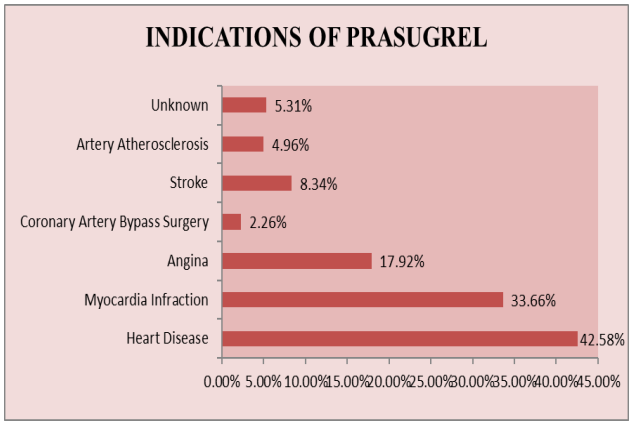

Figure 9: Classification of Indications and use for Prasugrel

DISCUSSION

This study is conducted on 110 patients, 64.02% of these patients were male and 36.08% of these patients were female. Most of patients were under Prasugrel therapy were in ages between 55 to 75 years old, where in Annie Guerin and Reema Mody study the median age of patients were 65 years old and it is done only on female patients. Also in Sheng-Feng Lin study, most age of patients were around 65 years old and male population were more than females, and in Nehad J. Ahmed study the majority of the patients who received Prasugrel were in the ages between 50 to 69. Based on this data we can achieve that mostly patients are exposed top Prasugrel use by any reason are mostly in ages between 50 to 70 years old. Most past and present diseases of patients were cardiovascular diseases Infection Diseases; where in most of studies reviewed for our study cardiovascular conditions were the most popular diseases. About interactions, 29.36 % interactions identified with Prasugrel (37 patients) 74.32% of

them classified within male and 25.67% of them into female. Therefore males were more incidences to show interactions of Prasugrel; other condition like their population of disease and treatment or multiple diseases could be effective on this percentage. Most interactions were between Prasugrel and Pantoprazole, Omeprazole and Aspirin; which could be because of their high significant and helpful need on treatment charts. Based on the our evaluation in this study on interaction with use of scales, 11.05% were identify as severe interactions, 53.81% were classify and identify as moderate in their interactions and 34.13% were classify as mild in their interactions. Based on their possibility of relation the effect and interactions, whereas we found that 17.62% of interactions were defined, 60.46% of interactions were probable and 22.91% of them were possible. Therefore we achieved that most of these interaction also could be affected by other situations as disease, foods, environments or drugs. Mechanisms of these interactions mostly were the increasing or decreasing of other drug among two drugs which could be because of same specific enzymes such as CYP2C19, CYP1A2, CYP2B6, CYP2C9 and CYP3A4 . Prasugrel used for several indication as Heart Disease (42.58%), Myocardia Infraction (33.66%), Angina (17.92%), Coronary Artery Bypass Surgery (2.26%), Stroke (8.34%), Artery, Atherosclerosis (4.96%) and other unknown condition (5.31%) . where in a study identified in both groups, more than three-quarters of patients had signs of additional ischemic heart disorders (75.9% and 80.3%, respectively), and 37.5% and 42.7%, respectively, had experienced a recent stroke. Prasugrel was mostly employed for the post-percutaneous coronary intervention period (32%) and secondary prevention of ischemic heart disease (60%). A noteworthy percentage of patients (31%) were administered Prasugrel in violation of the prescribed guidelines.

CONCLUSION

According to data collected in this study and its compare to other study, Prasugrel were use in patients with ages between 55 to 75 years old more in males and with most past and present diseases of cardiovascular diseases. One of four patients had Prasugrel interactions with other drugs, where mostly found in male than females. Available data suggest that pantoprazole is the PPI most likely to have a significant interaction with Prasugrel. Pantoprazole should be used since it is the PPI least likely to interact with Prasugrel but caution should be exercised in the concomitant. It's possible that doctors were more likely to prescribe Prasugrel combo therapy or to switch patients to a drug that was already accessible but still in the study stage. Prasugrel was mostly taken by itself, without combination, and was used often. It is crucial to prescribe it correctly, and before dispensing it, chemists have an obligation to ensure that it is appropriate for the patient and to look for any drug interactions.

Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

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REFERENCES

[1] A Guerin, R Mody, V Carter, C Ayas, H Patel, and K Lasch. Changes in Practice Patterns of Prasugrel in Combination with Proton Pump Inhibitors after an FDA Safety Communication. PLoS ONE, 11(1):e0145504, 2016.

[2] R Petty, and J Silcock. Explanations for variations in Prasugrel prescribing in England. Medicines Management and Pharmacy Practice Group, School of Healthcare, University of Leeds. Journal of Public Health, 30(4):494 498, 2008.

[3] N B Norgard, K D Mathews, and G C Wall. Drug–Drug Interaction Between Prasugrel and the Proton Pump Inhibitors. Annals of Pharmacotherapy, 43:1266-1274, 2009.

[4] P A Kubler, P I Pillans, M C Marrinan and M Frogley. Concordance between Prasugrel use and prescribing guidelines. Department of Clinical Pharmacology, Princess Alexandra Hospital and Pharmacy Department, University of Queensland, Brisbane, Queensland, Australia. Internal Medicine Journal, 34:663–667, 2004

[5] T K Ma, Y Y Lam, and V P Tan. Impact of genetic and acquired alteration in cytochrome P450 system on pharmacologic and clinical response to Prasugrel.

Pharmacological Therapeutics, 125:249–259, 2010.

[6] I Ben-Dor, N S Kleiman, and E Lev. Assessment, mechanisms, and clinical implication of variability in platelet response to aspirin and Prasugrel therapy. American Journal of Cardiology 2009;104:227–233.

[7] P Buonamici, R Marcucci, A Migliorini, G F Gensini, A Santini, and R Paniccia. Impact of platelet reactivity after Prasugrel administration on drug-eluting stent thrombosis. Journal of the American College of Cardiology, 49:2312–2317, 2007.

[8] M J Price, P B Berger, and P S Teirstein. Standard- vs high-dose Prasugrel based on platelet function testing after percutaneous coronary intervention: The GRAVITAS randomized trial. JAMA, 305:1097–1105, 2011.

[9] C Patrono, C Baigent, J Hirsh, and G Roth. Antiplatelet drugs: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th edition). Chest, 133:199S–233S, 2008.

[10] M Lordkipanidze, C Pharand, and T A Nguyen. Comparison of four tests to assess inhibition of platelet function by Prasugrel in stable coronary artery disease patients. European Heart Journal, 29:2877–2885, 2008.

[11] P Gurbel, K Bliden, and W Samara. Prasugrel effect on platelet reactivity in patients with stent thrombosis: results of the CREST Study. Journal of the American College of Cardiology, 46:1827-1832, 2005.

[12] J L Mega, S L Close, and S D Wiviott. Cytochrome p- 450 polymorphisms and response to Prasugrel. New England Journal of Medicine, 360:354-362, 2009.

[13] H Mani, S W Toennes, and B Linnemann. Determination of Prasugrel main metabolite in plasma: a useful tool for monitoring therapy? Their Drug Monitor, 30:84-89, 2008.

[14] M S Sabatine, C P Cannon, and C M Gibson. Effect of Prasugrel pretreatment before percutaneous coronary intervention in patients with ST-elevation myocardial infarction treated with fibrinolytics: the PCICLARITY study. JAMA, 294:1224–1232, 2005.

[15] H C Diener, J Bogousslavsky, and L M Brass. Aspirin and Prasugrel compared with Prasugrel alone after recent ischaemic stroke or transient ischaemic attack in highrisk patients (MATCH): randomised, double-blind, placebo-controlled trial. Lancet, 364:331–337, 2004.

[16] J S Li, E Yow, and K Y Berezny. Optimal dose of Prasugrel for platelet inhibition in children: primary results of the PICOLO Trial. Circulation, 117(4):553–559, 2008.

[17] CAPRIE Steering Committee. A randomised, blinded, trial of Prasugrel versus aspirin in patients at risk of ischaemic events (CAPRIE). Lancet, 348:1329–1339, 1996.

[18] Y Takahashi, Y Nishida, T Nakayama, and S Asai. Comparative effect of Prasugrel and aspirin versus aspirin alone on laboratory parameters: A retrospective, observational, cohort study. Cardiovascular Diabetology, 12:87, 2013.